(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, CO_2R^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, C_1-C_4 alkyl and benzyl;

(ii) an oligopeptide of 1 to 5 amino acids or a peptidomimetic molecule having substantially similar binding properties as the oligopeptide;

(iii) C_3-C_6 cycloalkyl, C_6-C_{10} bicycloalkyl, C_3-C_7 cycloalkylmethyl, or C_7-C_{10} arylalkyl, which may be additionally substituted with R^{11} as defined above;

R_3 is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain or O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids, an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, amino, carboxyl and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy or halogen;

(ii) hydrogen; and

(iii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl, or C_1,-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydroxy, halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, carbamido, cyano, keto, vinyl, sulfoxide, nitro, C_1[,]-C_3 alkylsulfonyl, or sulfone; and

(iii) C_1[,]-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide of 1 to 3 amino acids or a peptidomimetic;

alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

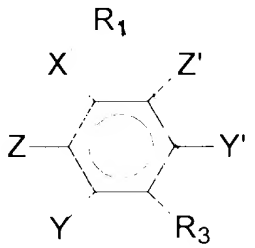
(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen.

12. (Once Amended) [The] A method [of] according to claim 8, wherein the picornavirus species is a rhinovirus species.

13. (Twice Amended) A method for [the treatment of a disease caused by a picornavirus species,] inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C=O;

R_1 is $-CF_3$;

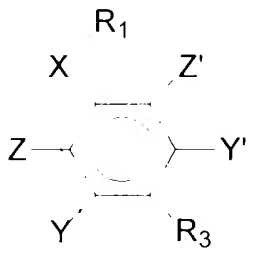
Z and Z are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $-CF_3$, –F, –CN, –COOH, $-SO_3H$, $-SO_2NH_2$ and $-CONH_2$. [; and

and Z′ and R_1 cannot form a ring.]

14. (Twice Amended) A method for [the treatment of a disease caused by a picornavirus species,] inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C=O;

R_1 is $–CF_3$;

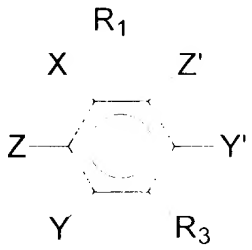
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $–CF_3$, –F, –CN, –COOH, $–SO_3H$, $–SO_2NH_2$ and $–CONH_2$; [; and

and Z and R_1 cannot form a ring.]

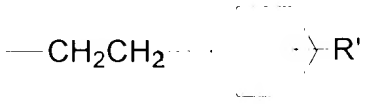
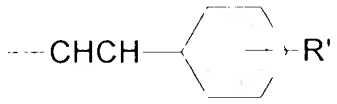
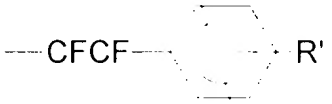
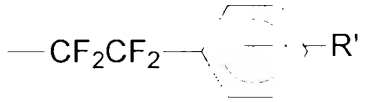
15. (Twice Amended) A method for [the treatment of a disease caused by a picornavirus species,] inhibiting picornaviral replication in a subject, wherein said compound



has the formula:

wherein X is –C=O;

R_1 is H, $–CH_3$, $–CF_3$, $CH_3–CH_2–CH_2–CH_2–CH_2–$, $CH_3–CH_2–$, $CH_3–CH_2–CH_2–$, $CF_3–CF_2–CF_2–CF_2–CF_2–$, –NH–R′′or one of the following phenyl groups

wherein R′ is –OH, $–NH_2$, –COOH, or $–COCH_3$ and R′′ is –OH, $–NH_2$, $–OCH_3$ and $–OCH_2CH_3$;

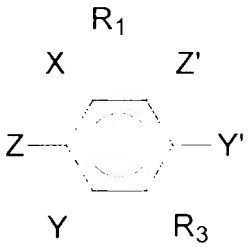
Z and Z′ are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are $–CF_3$[; and

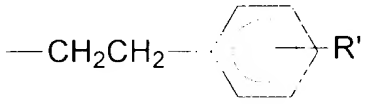
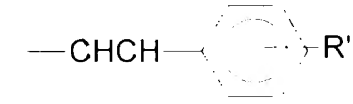
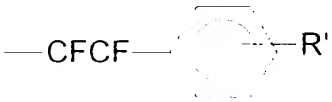
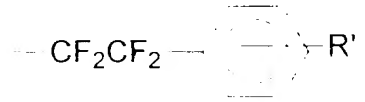
and Z′ and R_1 cannot form a ring.]

16. (Twice Amended) A method for [the treatment of a disease caused by a picornavirus species.] inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C(=O);

R_1 is H, $–CH_3$, $–CF_3$, $CH_3–CH_2–CH_2–CH_2–CH_2–$, $CH_3–CH_2–$, $CH_3–CH_2–CH_2–$, $CF_3–CF_2–CF_2–CF_2–CF_2–$, –NH–R′′, or one of the following phenyl groups

wherein R′ is –OH, $–NH_2$, –COOH, or $–COCH_3$ and R′′ is –OH, $–NH_2$, $–OCH_3$ and $–OCH_2CH_3$;

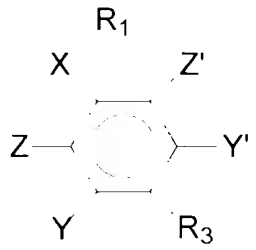
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen; and

Y and Y′ are $–CF_3$; [; and

and Z′ and R_1 cannot form a ring.]

17. (Once Amended) A method [for the treatment of a disease caused by a picornavirus species.] of inhibiting picornaviral replication in a subject, wherein said [compound has] method includes the use of a compound with the formula:



X is selected from the group consisting of –C=O-, -S=O-, and -C=S-;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, C_1-C_4 alkyl and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids, an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, amino, carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z′ is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y′ are independently selected from the group consisting of:

(i) halogen, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

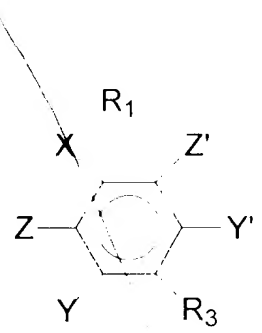
(ii) carbamyl, carbamido, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, and sulfone; and

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide of 1 to 3 amino acids or a peptidomimetic;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen.

18. (New Claim) -- A method of inhibiting picornaviral replication in a subject, comprising the step of administering an effective amount of a compound having a formula:



wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)-NH, (C=O)-O and (C=O)-S:

R_1 is selected from the group consisting of:

(i) hydrogen, hydroxyl or a hydrocarbon chain [of] from [about] 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said hydrocarbon chain is unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, CO_2R^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, C_1-C_4 alkyl and benzyl;

(ii) an oligopeptide of 1 to 5 amino acids or a peptidomimetic molecule having substantially similar binding properties as the oligopeptide;

(iii) C_3-C_6 cycloalkyl, C_6-C_{10} bicycloalkyl, C_3-C_7 cycloalkylmethyl, or C_7-C_{10} arylalkyl, which may be additionally substituted with R^{11} as defined above;

R_3 is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain or O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids, an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, amino, carboxyl and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy or halogen;

(ii) hydrogen; and

(iii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl, or C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydroxy, halogen, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, or hydrogen except that Y and Y' cannot be hydrogen simultaneously;

(ii) carbamyl, carbamido, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone; and

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide of 1 to 3 amino acids or a peptidomimetic;

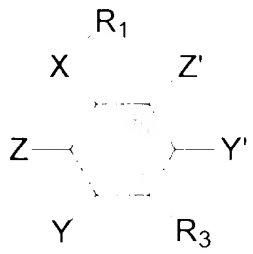
alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen.

19. (New Claim) -- A method of inhibiting picornaviral replication in a subject, wherein said method includes the use of a compound with the formula:



X is selected from the group consisting of –C=O-, -S=O-, and -C=S-;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C=OR^{13})$, SO_2R^{14}, SOR^{14}, $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, C_1-C_4 alkyl and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids, an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, amino, carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z′ is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y′ are independently selected from the group consisting of:

(i) halogen, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, or hydrogen except that Y and Y' cannot be hydrogen simultaneously;

(ii) carbamyl, carbamido, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, and sulfone; and

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide of 1 to 3 amino acids or a peptidomimetic;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen. --

REMARKS

Claims 8 and 12-17 are pending in the application. Applicants have amended claims 8 and 12-17, and added new claims 18-19.

35 U.S.C. §112, FIRST PARAGRAPH REJECTION OF CLAIMS 8 AND 12-17

The Examiner has rejected claims 8 and 12-17 on the grounds that they are not enabled by the specification. The Examiner has suggested amendments to these claims to overcome the §112, first paragraph rejections. Claims 8 and 12-17 have been amended according to the Examiner's suggestion. Therefore, it is respectfully submitted that such claims are patentable, having overcome this rejection.